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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,299	02/06/2006	Heribert Hellstern	ON/4-33308A	6687

1095 7590 06/06/2008

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
LUKTON, DAVID	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
06/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,299	HELLSTERN ET AL.	
	Examiner	Art Unit	
	DAVID LUKTON	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *3-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Pursuant to the response filed 3/5/08, claim 1 has been amended. Claims 1-6 remain pending. Claims 3-6 remain withdrawn from consideration.

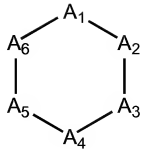
The following is a quotation of 35 USC, §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1-2 are rejected under 35 U.S.C. §103 as being unpatentable over Bruns (*Eur J. Endocrinol* **146**, 707, 2002).

Bruns discloses the elected specie. Bruns does not provide a synthetic method

The claims are drawn to methods of producing a cyclic hexapeptide. A cyclic hexapeptide can be represented as follows, where each of A_1, A_2 (etc.) represents an amino acid residue:

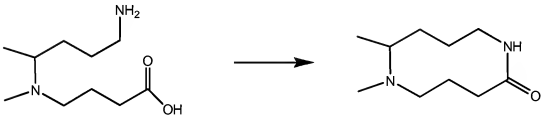


For a cyclic hexapeptide, there are six peptides which, upon cyclization, will yield the target compound. They are the following:

A_1-A_2-A_3-A_4-A_5-A_6	1
A_2-A_3-A_4-A_5-A_6-A_1	2
A_3-A_4-A_5-A_6-A_1-A_2	3
A_4-A_5-A_6-A_1-A_2-A_3	4
A_5-A_6-A_1-A_2-A_3-A_4	5
A_6-A_1-A_2-A_3-A_4-A_5	6

Via instant claim 1, applicants have chosen one of the six possibilities. At most, there are only six possibilities to begin with. Furthermore, consider the case where A_1 represents proline. If A_1 represents proline, then the first two linear hexapeptide precursors would be recognized as the least desirable for a "head-to-tail" cyclization. The reason why precursor peptides 3-6 would be viewed as superior is that they take

advantage of the reduction in the "degrees of freedom" afforded by the proline. Consider the following two reactions:



The physical organic chemist of ordinary skill would expect the first of these to be more facile than the second, owing to the greater number of "degrees of freedom" (in simplistic terms, "floppiness") of the aminopropane and butyric acid groups in the second of the two reaction precursors as compared to the first. Thus, turning back to the cyclic peptide at issue, one would expect a more facile cyclization for hexapeptide precursor such as A_4-A_5-A_6-A_1-A_2-A_3 as compared with A_2-A_3-A_4-A_5-A_6-A_1 (again A_1 representing proline). Thus, the choice is then among four peptides, rather than six. Given four possibilities, it is difficult to argue that any is unobvious.

Applicants have argued that when the cyclization (using HBTU, method (b)) occurred between amino acids 4 and 5, the yield was 77%, whereas for the cyclization between amino acids 5 and 6, the yield was only 20%. However, it remains the case that there are only four principle cyclization precursors, and that none of them is unobvious. What is also true is that claim 1 is not limited to cyclization by HBTU. Thus, maybe it is true that for this particular reagent some advantage accrues when cyclizing between amino acids 4 and 5, but it does not necessarily follow that cyclization between amino acids 4 and 5 provides better yields than for the other three precursor possibilities regardless of what reagent is used.

The rejection is maintained.

Claims 1-2 are rejected under 35 U.S.C. §103 as being unpatentable over Bruns (*Eur J. Endocrinol* **146**, 707, 2002) in view of Blackburn, Christopher (*Methods in Enzymology* **289**, 175-198, 1997)

As indicated previously, Bruns discloses the elected specie, but does not provide a synthetic method. Blackburn discloses methods of preparing cyclic peptides; Blackburn, however, does not disclose the peptide which is the "target" of the instant claims. It would have been obvious to the peptide chemist of ordinary skill to employ one of the synthesis methods described therein.

Claims 1-2 are rejected under 35 U.S.C. §103 as being unpatentable over Albert (US 2005/0014686) in view of Blackburn, Christopher (*Methods in Enzymology* **289**, 175-198, 1997).

Albert discloses the elected specie. Blackburn discloses methods of cyclizing peptides

It would have been obvious to the peptide chemist of ordinary skill to employ one of the synthesis methods described therein.

✧

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

/David Lukton/

Primary Examiner, Art Unit 1654